

REMARKS

Identical paper and computer readable forms of the Sequence Listing in the present application were submitted in the parent application, 09/543,668, filed April 7, 2000. Pursuant to 37 C.F.R. § 1.821(e), Applicants request that the computer readable form submitted in the parent application be used in lieu of filing a duplicate computer readable form with this application.

Applicants hereby authorize the filing fee of \$463 to be charged to Deposit Account 081930. Please debit any underpayment or credit any overpayment to Deposit Account No. 081930.

Pending Claims 27-47 of the application are believed to be in condition for allowance. In the event the Examiner has any questions regarding this application, the Examiner is invited to contact the Applicants' undersigned representative.

Respectfully submitted,

Dated: November 21, 2001



Timothy L. McCutcheon, Esq.
Registration No. 41,184
Heska Corporation
1613 Prospect Parkway
Fort Collins, Colorado 80525
Telephone: (970) 493-7272
Facsimile: (970) 491-9976

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

On page 1, the paragraph entitled "Cross-Reference to Related Applications" was amended as follows --This application is a divisional of copending U.S. Application Serial Number 09/543,668, filed April 7, 2000, which claims priority to U.S. Provisional Patent Application Serial Number 60/128,704, filed April 9, 1999, each entitled "FLEA HEAD, NERVE CORD, HINDGUT AND MALPIGHIAN TUBULE NUCLEIC ACID MOLECULES, PROTEINS AND USES THEREOF", filed April 9, 1999.--

The paragraph spanning page 170, line 14 through page 171, line 12 was amended as follows: --A nucleic acid molecule comprising nucleotides 59 through 827 of SEQ ID NO:7, encoding a predicted mature flea chitin-binding protein, was PCR amplified from the pBluescript™ clone described above as the template, using sense primer CBP-FE, having nucleotide sequence 5' **CGG GAT CCT** GCT GAC AGG AAT TCG CCC AC 3', having a *Bam*HI site indicated in bold, designated herein as SEQ ID NO:[39]51, and anti-sense primer CBP-RE, having nucleotide sequence 5' CAT **GGT ACC** CCT GGT TTA AGC CTT ACT TAG C 3', having a *Kpn*I site indicated in bold, designated herein as SEQ ID NO:[38]52. PCR reactions were performed using standard PCR reaction and thermocycling conditions described in Example 4. The PCR product was digested with *Bam*HI and *Kpn*I and ligated into the vector pTrcHisB, available from Invitrogen, that had been digested with *Bam*HI and *Kpn*I and treated with alkaline phosphatase. The resulting recombinant molecule, referred to herein as pTrc-nCfCBP₇₆₉, was transformed into *E. coli* strain BL21, available from Novagen, to form recombinant cell *E. coli*:pTrc-nCfCBP₇₆₉. The recombinant cell was grown under standard conditions and then incubated in the presence of 0.5 μM IPTG to induce expression of recombinant protein, predicted to be a protein of approximately 32 kDa. Expression of protein was confirmed using Coomassie-blue-stained Tris-glycine gel and by Western blot using a T7 tag antibody which showed expression of an about 32-kDa protein. The protein product was purified by liquid chromatography using a HiTrap™ chelating column charged with NiCl₂, available from Pharmacia, and was shown to contain the His tag of the vector when subjected to automated protein sequencing by Edman degradation."

IN THE CLAIMS

Claims 1-26 were canceled without prejudice or disclaimer of the subject matter thereof.

Claims 27-47 were added as follows:

27. An isolated *C. felis* cDNA molecule or a *C. felis* RNA molecule nucleic acid molecule selected from the group consisting of (a) a *C. felis* cDNA molecule or a *C. felis* RNA molecule that hybridizes to a polynucleotide selected from the group consisting of SEQ ID NO:1874 and SEQ ID NO:1876 under conditions comprising (1) hybridizing in a solution comprising 1X SSC in the absence of helix destabilizing compounds, at a temperature of about 37°C and (2) washing in a solution comprising 1X SSC and in the absence of helix destabilizing compounds, at a temperature of about 47.5°C, wherein said isolated nucleic acid molecule encodes a protein having chloride channel activity; and (b) a *C. felis* cDNA molecule or a *C. felis* RNA molecule comprising a nucleic acid sequence fully complementary to a nucleic acid molecule of (a).

28. The nucleic acid molecule of Claim 27, wherein said nucleic acid molecule is selected from the group consisting of: a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1872, SEQ ID NO:1874, SEQ ID NO:1875 and SEQ ID NO:1876; and fragments thereof, wherein said fragment comprises at least 25 contiguous nucleotides from a nucleic acid sequence selected from the group consisting of SEQ ID NO:1872, SEQ ID NO:1874, SEQ ID NO:1875 and SEQ ID NO:1876.

29. The nucleic acid molecule of Claim 27, wherein said nucleic acid molecule encodes a protein comprising amino acid sequence SEQ ID NO:1873 and nucleic acid molecules encoding a variant thereof that is at least 95% identical to SEQ ID NO:1873, wherein said variant protein has chloride channel activity.

30. The nucleic acid molecule of Claim 27, wherein said nucleic acid molecule encodes a protein comprising amino acid sequence SEQ ID NO:1873.

31. A recombinant molecule comprising a nucleic acid molecule as set forth in Claim 27 operatively linked to a transcription control sequence.

32. A recombinant virus comprising a nucleic acid molecule as set forth in Claim 27.

33. A recombinant cell comprising a nucleic acid molecule as set forth in Claim 27.

34. A method to produce a protein encoded by an isolated nucleic acid molecule selected from the group consisting of a *C. felis* cDNA molecule and a *C. felis* RNA molecule that hybridizes to a polynucleotide selected from the group consisting of SEQ ID NO:1874 and SEQ ID NO:1876, under conditions comprising (a) hybridizing in a solution comprising 1X SSC in the absence of helix destabilizing compounds, at a temperature of about 37°C and (b) washing in a solution comprising 1X SSC in the absence of helix destabilizing compounds, at a temperature of about 47.5°C, wherein said isolated nucleic acid molecule encodes a protein having chloride channel activity, said method comprising the steps of (1) culturing a cell transformed with said isolated nucleic acid molecule encoding said protein operatively linked to a transcription control sequence and (2) recovering said encoded protein.

35. The method of Claim 34, wherein said nucleic acid molecule encodes a protein having amino acid sequence SEQ ID NO:1873.

36. The method of Claim 34, wherein said nucleic acid molecule is selected from the group consisting of: a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1872 and SEQ ID NO:1875; and fragments thereof, wherein said fragment comprises at least 25 contiguous nucleotides from a nucleic acid sequence selected from the group consisting of SEQ ID NO:1872 and SEQ ID NO:1875.

37. A composition comprising an excipient and an isolated *C. felis* cDNA molecule or a *C. felis* RNA molecule nucleic acid molecule selected from the group consisting of (a) a *C. felis* cDNA molecule or a *C. felis* RNA molecule that hybridizes to a polynucleotide selected from the group consisting of SEQ ID NO:1874 and SEQ ID NO:1876 under conditions comprising (1) hybridizing in a solution comprising 1X SSC in the absence of helix destabilizing compounds, at a temperature of about 37°C and (2) washing in a solution comprising 1X SSC and in the absence of helix destabilizing compounds, at a temperature of about 47.5°C, wherein said isolated nucleic acid molecule encodes a protein having chloride channel activity; and (b) a *C. felis* cDNA molecule or a *C. felis* RNA molecule comprising a nucleic acid sequence fully complementary to a nucleic acid molecule of (a).

38. The composition of Claim 37, wherein said composition further comprises a component selected from the group consisting of an adjuvant and a carrier.

39. An isolated protein encoded by a *C. felis* cDNA molecule or a *C. felis* RNA molecule that hybridizes to a nucleic acid sequence selected from the group consisting of SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:24, SEQ ID NO:27, SEQ ID NO:30, SEQ ID NO:33, SEQ ID NO:36, SEQ ID NO:39, SEQ ID NO:42, SEQ ID NO:45, SEQ ID NO:48, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, SEQ ID NO:170, SEQ ID NO:1860, SEQ ID NO:1863, SEQ ID NO:1866, SEQ ID NO:1869, SEQ ID NO:1871, SEQ ID NO:1874, SEQ ID NO:1876, SEQ ID NO:1907, SEQ ID NO:1909, SEQ ID NO:1911, SEQ ID NO:1913, SEQ ID NO:1916, SEQ ID NO:1918, SEQ ID NO:1921, SEQ ID NO:1923, SEQ ID NO:1926, SEQ ID NO:1928, and SEQ ID NO:1931, under conditions comprising (1) hybridizing in a solution comprising 1X SSC in the absence of helix destabilizing compounds, at a temperature of about 37°C and (2) washing in a solution comprising 1X SSC and in the absence of helix destabilizing compounds, at a temperature of about 47.5°C, wherein said isolated protein has chloride channel activity.

40. The protein of Claim 39, wherein said protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:20, SEQ ID NO:26, SEQ ID NO:32, SEQ ID NO:38, SEQ ID NO:44, SEQ ID NO:154, SEQ ID NO:160, SEQ ID NO:163, SEQ ID NO:169, SEQ ID NO:1862, SEQ ID NO:1868, SEQ ID NO:1915, SEQ ID NO:1920, SEQ ID NO:1925, and SEQ ID NO:1930.

41. A composition comprising an excipient and an isolated protein of Claim 39.

42. An isolated antibody that selectively binds to a protein as set forth in Claim 39.

43. A composition comprising an excipient and an isolated antibody of Claim 42.

44. A method to identify a compound capable of inhibiting activity of an isolated protein of Claim 39, said method comprising contacting an isolated protein of Claim 39 with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has activity; and determining if said putative inhibitory compound inhibits said activity.

45. A kit to identify a compound capable of inhibiting activity of an isolated protein of Claim 39, said test kit comprising an isolated protein of Claim 39 and a means for determining the extent of inhibition of said activity in the presence of a putative inhibitory compound.

46. An isolated nucleic acid molecule expressed by a tissue selected from the group consisting of a flea HMT tissue and a flea HNC tissue, identified by a method comprising: (a) constructing a cDNA library enriched for HMT or HNC expressed sequences; and (b) identifying a nucleic acid molecule in said library.

47. The nucleic acid molecule of Claim 46, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:170, SEQ ID NO:1859, SEQ ID NO:1860, SEQ ID NO:1861, SEQ ID NO:1863, SEQ ID NO:1864, SEQ ID NO:1866, SEQ ID NO:1867, SEQ ID NO:1869, SEQ ID NO:1870, SEQ ID NO:1871, SEQ ID NO:1905, SEQ ID NO:1906, SEQ ID NO:1907, SEQ ID NO:1908, SEQ ID NO:1909, SEQ ID NO:1910, SEQ ID NO:1911, SEQ ID NO:1912, SEQ ID NO:1913, SEQ ID NO:1914, SEQ ID NO:1916, SEQ ID NO:1917, SEQ ID NO:1918, SEQ ID

NO:1919, SEQ ID NO:1921, SEQ ID NO:1922, SEQ ID NO:1923, SEQ ID NO:1924, SEQ ID NO:1926, SEQ ID NO:1927, SEQ ID NO:1928, SEQ ID NO:1929, SEQ ID NO:1931, and a nucleic acid sequence of Table I, a nucleic acid sequence of Table II, a nucleic acid sequence of Table III, and a nucleic acid sequence of Table IV.

FIG. 1